

Please replace the paragraph beginning on page 34, line 10, with the following amended paragraph:

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There are several ways of overcoming this limitation. The easiest is to make the contour resistor a two-terminal device by adding a conductor, which is terminated to ground, at its outbound edge (opposite the channel). This would allow a very wide lateral width at the anode and a very narrow lateral width at the cathode. The disadvantage of this method is the increase in power dissipation and voltage break down at the anode end. A second method is to decrease the incremental resistance of the contour resistor by increasing the thickness of the thick film resistor as it approaches the cathode, but this would require very unusual screening techniques to lay down such a structure. A third method, illustrated in FIG. 10, is to apply overlapping geometries of decreasing resistivity inks such that at the cathode end 108 of the contour resistor 4642 has a low resistivity and the anode end 106 has a high resistivity with a resistivity gradient between the two ends. The precise voltage profile is then achieved by laser trimming the outboard sides 110, 112 of the geometries. A fourth method is to use ink jet technology to deposit the varying resistivity ink directly from three or four ink resistivities, which are applied using a computer controller to produce the desired resistance gradient. This can be followed by laser trimming. This last approach can also limit the width of the contour resistor to less than half a channel width. For limited resistor excursions of less than an octave, single resistivity ink is adequate but would still require laser trimming. All four of the forgoing exemplary embodiments contemplate fabrication by screen printing, but the concepts can be implemented using other known fabrication techniques.

The following listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

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1. (original) A liquid-phase electromobility focusing separation system configured to separate at least one discrete analyte species from an analyte sample, comprising:

a first separation channel defined by a confinement enclosing an interior channel volume, said first separation channel having first and second ends and a longitudinal axis, and

said first separation channel being configured to contain an electrolyte solution within the interior channel volume, said separation channel providing the only flowpath for both the analyte sample and the electrolyte solution;

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a continuous electric field intensity gradient generator configured to apply a electric field intensity gradient within the first separation channel along the longitudinal axis over at least a portion of the first separation channel intermediate the first and second ends, the intensity of electric field generated varying as a continuous function of location along the longitudinal axis, whereby electrophoretic migration of an analyte species within the first separation channel is actuated by a force that varies with position along the longitudinal axis as a continuous function of position along the longitudinal axis within said portion of the first separation channel;

an electroosmotic flow generator configured to generate an electroosmotic flow along the longitudinal axis of the first separation channel, which electroosmotic flow is variable as to at least one of: (i) the magnitude of the flow, and (ii) the direction of the flow, to enhance separation of said at least one analyte species by enabling separation control of an interaction of forces it created by the continuous electric field intensity gradient generator and the electroosmotic flow generator.

2. (original) A system as in claim 1, wherein the electroosmotic flow generator comprises a power supply and a distributed source of potential positioned adjacent said containment, whereby zeta potential of an interior surface in fluid contact with the first separation channel can be altered by at least one of:

- a) applying a potential, and
- b) altering at least one of (i) the magnitude, and (ii) polarity, of potential applied, to the distributed source of potential from the power supply.

3. (original) A system as in claim 1, wherein the continuous electric field intensity gradient generator further comprises:

a cathode positioned adjacent one of the first and second ends of the first separation channel;

an anode positioned adjacent the other of the first and second ends of the first separation channel;

a power supply in electric communication with the cathode and the anode;

a continuously varying resistor in fluid communication with the first separation channel along at least a portion of the longitudinal axis intermediate the first and second ends, said resistor having a resistance that varies as a continuous function of position along the longitudinal axis of the first separation channel, whereby an electric potential in the electrolyte fluid varies as a non-linear continuous function of position along the longitudinal axis of the first separation channel and, as a result, the electric field intensity varies as a continuous function of position along the longitudinal axis over at least a portion of the first separation channel intermediate the first and second ends.

4. (currently amended to change dependency) A system as in claim 2 3, wherein the continuous electric field intensity gradient generator comprises a continuously varying resistor comprising a contour resistor in fluid communication with the first separation channel along at least a portion of the longitudinal axis intermediate the first and second ends, said resistor having a resistance that varies as a continuous function of position along the longitudinal axis of the first separation channel, whereby an electrical potential in the electrolyte fluid varies as a non-linear continuous function of position along the longitudinal axis of the first separation channel and, as a result, the electric field intensity varies as a

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continuous function of position along the longitudinal axis over at least a portion of the first separation channel intermediate the first and second ends.

5. (original) A system as in claim 4, wherein the continuously varying resistor comprises a filament within the first separation channel.

6. (original) A system as in claim 4, wherein the continuously varying resistor comprises a packing within the first separation channel that varies in resistivity as a continuous function of position along the longitudinal axis.

7. (currently amended to change dependency) A system as in claim 4 3, wherein said contour resistor comprises a conductive material having a cross sectional shape which varies as a continuous function of position along the longitudinal axis.

8. (currently amended to change dependency) A system as in claim 4 3, wherein said contour resistor has a material property that varies as a continuous function of position along said longitudinal axis.

9. (original) A system as in claim 1, further comprising an electrolyte solution disposed in the first separation channel.

10. (original) A system as in claim 9, wherein the electrolyte solution comprises a buffer solution.

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11. (original) A system as in claim 9, further comprising a gel disposed in the first separation channel.

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12. (original) A system as in claim 9, further comprising a polymeric solution disposed in the first separation channel.

13. (original) A system as in claim 9, further comprising a micellular dispersion disposed in the first separation channel.

14. (original) A system as in claim 1, wherein the containment is configured to provide a high aspect substantially rectangular cross-sectional shape for the first separation channel.

15. (original) A system as in claim 14, wherein the electroosmotic flow generator comprises a first plate disposed adjacent one side of the containment and configured to alter the zeta potential on an interior surface of the first separation channel adjacent the first side of the containment and a second plate adjacent a second side of the containment configured to alter the zeta potential on an interior surface of the containment adjacent the second side of the containment.

16. (original) A system as in claim 1, further comprising a first orientation electric field generator.

17. (original) A system as in claim 16, wherein the first orientation electric field generator

comprises an electroosmotic flow generator further comprising a first plate disposed adjacent one side of the containment and configured to alter the zeta potential on an interior surface of the first separation channel adjacent the first side of the containment and a second plate adjacent a second side of the containment configured to alter the zeta potential on an interior surface of the containment adjacent the second side of the containment, wherein the first plate and the second plate are brought to different potentials so as to create an alignment electric field configured to align bipolar molecules in directions normal to the first and second plates.

18. (original) A system as in claim 16, wherein the orientation electric field oscillates at a selected frequency.

19. (original) A system as in claim 16, further comprising a second orientation electric field generator configured for generating a second orientation electric field acting in a direction normal to the first orientation electric field, wherein the first and second orientation electric fields can be varied to orient bipolar molecules to a selected orientation by cooperation between the first and second orientation alignment electric fields.

20. (original) A system as in claim 1, further comprising a detector configured for detecting analyte species in said first separation channel, said detector being positioned intermediate the first and second ends of said first separation channel.

21. (currently amended) A system as in claim 20, further comprising:

a steering valve in fluid communication with the first separation channel, said

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steering valve comprising a connecting channel and configured to selectively divert fluid containing analyte species from said first separation channel at a location intermediate the first and second ends of the first separation channel into the connecting channel;

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a second separation channel adapted for containing electrolyte fluid and analyte species, said second separation channel having a longitudinal axis and a first end and a second end, said second separation channel being in fluid communication with the connecting channel of said steering valve at a location intermediate said first and second ends, and, ~~said second separation channel further comprising a second~~

an electric field generator configured for moving analyte species along the second separation channel by at least one of electrophoretic migration and electroosmotic flow.

22. (original) A system as in claim 21, further comprising an analyte concentrator located in said second separation channel intermediate the first and second ends.

23. (original) A system as in claim 22, wherein said analyte concentrator comprises a line source of electro potential and an isolated ground, whereby an electric field generated by the second electric field generator can be locally altered so as to focus an analyte species at a location intermediate the first and second ends of the second separation channel.

24. (original) A system as in claim 23, further comprising a first electrode positioned at a first point along the longitudinal axis of the second separation channel, said first electrode being connected to said isolated ground, and a second electrode positioned at a second point along said longitudinal axis of the second separation channel, said second electrode being

connected to a source of potential, said source of electro potential being also connected to the isolated ground.

25. (original) The system of claim 24, further comprising an analyte species detector positioned intermediate said first electrode and said second electrode.

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26. (currently amended) An electromobility focusing separation system configured to separate analyte species in a fluid sample containing at least one analyte species, comprising:

a first separation channel defined by a containment forming a first elongated separation channel chamber having a longitudinal axis and first end and a second end, said containment configured to contain the fluid sample in the first elongated separation channel chamber,

an electrolyte solution contained within the first separation channel

an anode adjacent and in fluid communication with the first end of the first elongated separation channel chamber,

a cathode adjacent and in fluid communication with the second end of the first elongated separation channel chamber,

said containment and said electrolyte solution cooperating to provide a charge accumulation at interior wall surfaces of the first elongated separation channel chamber in response to an applied potential so as to give rise to bulk electroosmotic flow of the electrolyte solution,



a first power supply in electric communication with the anode and the cathode and configured to provide an electrical potential there between, whereby electrophoretic migration of analyte species and electroosmotic bulk flow of the electrolyte solution is enabled,

a sample injection port coupled to the separation channel, the sample injection port being in fluid communication with the electrolyte solution and enabling injection of a fluid sample containing one or more analyte species into the electrolyte solution,

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a resistor disposed parallel and in fluid communication with the first elongated separation channel chamber along at least a portion of said first elongated separation channel chamber intermediate the first and second ends thereof, said resistor having a variable resistance varying as a continuous function of position along the longitudinal axis of said first elongated separation channel chamber; and,

an ~~second~~ electric field generator configured to control the direction and velocity of the electroosmotic bulk flow of the electrolyte solution;

whereby electrophoretic migration of analyte species is effected by an electric field intensity which varies as a continuous function of position along the longitudinal axis of said first elongated separation channel chamber at locations adjacent the resistor, and electrophoretic migration of analyte species and electroosmotic bulk flow of the electrolyte solution can combine to separate analyte species along the longitudinal axis of the first elongated separation channel.

27. (original) A system as in claim 26, wherein the electroosmotic bulk flow is in a direction opposite to a direction of electrophoretic migration of analyte species of interest.

28. (currently amended) A system as in claim 26, wherein the electric field electroosmotic flow generator configured to control the direction and velocity of the electroosmotic bulk flow of the electrolyte solution comprises a power supply and a distributed source of potential positioned adjacent said containment on an exterior surface, whereby zeta potential of an interior surface in fluid contact with the first separation channel can be altered by at least one of:

a) applying a potential; and,

b) altering at least one of (i) the magnitude, and (ii) polarity, of potential applied to the distributed source of potential from the power supply.

29. (original) A system as in claim 26, wherein said resistor is a contour resistor in fluid communication with the first separation channel along at least a portion of the longitudinal axis intermediate the first and second ends, said resistor having a resistance that varies as a continuous function of position along the longitudinal axis of the first separation channel, whereby an electric potential in the electrolyte fluid varies as a non-linear continuous function of position along the longitudinal axis of the first separation channel, and as a result the electric field intensity varies as a continuous function of position along the longitudinal axis over at least a portion of the first separation channel intermediate the first and second ends.

30. (original) A system as in claim 26, wherein the resistor is a continuously varying resistor in fluid communication with the first separation channel along at least a portion of the longitudinal axis intermediate the first and second ends, said resistor having a resistance that varies as a continuous function of position along the longitudinal axis of the first separation channel, whereby an electric potential in the electrolyte fluid varies as a non-linear continuous function of

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position along the longitudinal axis of the first separation channel, and as a result the electric field intensity varies as a continuous function of position along the longitudinal axis over at least a portion of the first separation channel intermediate the first and second ends.

31. (original) A system as in claim 30, wherein the continuously varying resistor comprises a filament within the first separation channel.

32. (original) A system as in claim 30, wherein the continuously varying resistor comprises a packing within the first separation channel that varies in resistivity as a continuous function of position along the longitudinal axis.

33. (original) A system as in claim 29, wherein said contour resistor comprises a conductive material having a cross-sectional shape which varies as a continuous function of position along the longitudinal axis.

34. (original) A system as in claim 29, wherein said contour resistor has a material property that varies as a continuous function of position along said longitudinal axis.

35. (original) A system as in claim 26, further comprising an electrolyte solution disposed in the first separation channel.

36. (original) A system as in claim 35, wherein the electrolyte solution comprises a buffer solution.

37. (original) A system as in claim 35, further comprising a gel disposed in the first separation channel.

38. (original) A system as in claim 35, further comprising a polymeric solution disposed in the first separation channel.

39. (original) A system as in claim 35, further comprising a micellular dispersion disposed in the first separation channel.

40. (original) A system as in claim 26, wherein the containment is configured to provide a high aspect substantially rectangular cross-sectional shape for the first separation channel.

41. (currently amended) A system as in claim 40, wherein the electric field electroosmotic flow generator configured to control the direction and velocity of the electroosmotic bulk flow of the electrolyte solution comprises a first plate disposed adjacent one side of the containment and configured to alter the zeta potential on an interior surface of the first separation channel adjacent the first side of the containment and a second plate adjacent a second side of the containment configured to alter the zeta potential on an interior surface of the containment adjacent the second side of the containment.

42. (original) A system as in claim 26, further comprising a first orientation electric field generator.

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43. (original) A system as in claim 42, wherein the first orientation electric field generator comprises an electroosmotic flow generator further comprising

a first plate disposed adjacent one side of the containment and configured to alter the zeta potential on an interior surface of the first separation channel adjacent the first side of the containment, and

a second plate adjacent a second side of the containment configured to alter the zeta potential on an interior surface of the containment adjacent the second side of the containment, wherein the first plate and the second plate are brought to different potentials so as to create an alignment electric field configured to align bipolar molecules in directions normal to the first and second plates.

44. (original) A system as in claim 43 wherein the orientation electric field oscillates at a pre-selected frequency.

45. (original) A system as in claim 43, further comprising a second orientation electric field generator configured for generating a second orientation electric field acting in a direction normal to the first orientation electric field, wherein the first and second orientation electric fields can be varied to orient bipolar molecules to a selected orientation by cooperation between the first and second orientation alignment electric fields.

46. (original) A system as in claim 26, further comprising a detector configured for detecting analyte species in said first separation channel, said detector being positioned intermediate the first and second ends of said first separation channel.

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47. (currently amended) A system as in claim 46, further comprising:

a steering valve in fluid communication with the first separation channel, said steering valve comprising a connecting channel and configured to selectively divert fluid containing analyte species from said first separation channel at a location intermediate the first and second ends of the first separation channel into the connecting channel;

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a second separation channel adapted for containing electrolyte fluid and analyte species, said second separation channel having a longitudinal axis and a first end and a second end, said second separation channel being in fluid communication with the connecting channel of said steering valve at a location intermediate said first and second ends, and,  
~~said second separation channel further comprising a second~~

an electric field generator configured for moving analyte species along the second separation channel by at least one of electrophoretic migration and electroosmotic flow.

48. (original) A system as in claim 47, further comprising an analyte concentrator located in said second separation channel intermediate the first and second ends.

49. (original) A system as in claim 48, wherein said analyte concentrator comprises at least one line source of electro potential and an isolated ground, whereby an electric field generated by the second electric field generator can be locally altered so as to focus an analyte species at a location intermediate the first and second ends of the second separation channel.

50. (original) A system as in claim 49, further comprising a first electrode positioned at a first point along the longitudinal axis of the second separation channel, said first electrode being connected to said isolated ground, and a second electrode positioned at a second point along said longitudinal axis of the second separation channel, said second electrode being connected to a source of potential, said source of electro potential being also connected to the isolated ground.

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51. (original) The system of claim 50, further comprising an analyte species detector positioned intermediate said first electrode and said second electrode.

52. (currently amended) An electromobility focusing separation system configured to separate analyte species in a fluid sample containing at least one analyte species, comprising:

a first separation channel defined by a containment forming a first elongated separation channel chamber having a longitudinal axis and first end and a second end, said containment configured to contain the fluid sample in the first elongated separation channel chamber;

an electrolyte solution contained within the first separation channel,

said containment and said electrolyte solution cooperating to provide a charge accumulation at interior wall surfaces of the first elongated separation channel chamber so as to give rise to bulk electroosmotic flow of the electrolyte solution;

an anode adjacent and in fluid communication with the first end of the first elongated separation channel chamber;

a cathode adjacent and in fluid communication with the second end of the first elongated separation channel chamber;

a first power supply in electrical communication with the anode and the cathode and configured to provide an electrical potential there between, whereby electrophoretic migration of analyte species and electroosmotic bulk flow of the electrolyte solution is enabled;

a sample injection port intermediate the first and second ends of the separation channel, the sample injection port being in fluid communication with the electrolyte solution and enabling injection of a fluid sample containing one or more analyte species into the electrolyte solution;

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a contour resistor disposed parallel and in fluid communication with the first elongated separation channel chamber along at least a portion of said first elongated separation channel chamber intermediate the first and second ends thereof, said contour resistor having a variable resistance varying as a continuous function of position along the longitudinal axis of said first elongated separation channel chamber; and,

an ~~second~~ electric field generator configured to control the direction and velocity of electroosmotic bulk flow of the electrolyte solution, whereby electrophoretic migration of analyte species is effected by an electric field intensity which varies as a continuous function of position along the longitudinal axis of said first elongated separation channel chamber at locations adjacent the contour resistor, and electrophoretic migration of analyte species and electroosmotic bulk flow of the electrolyte solution can combine to separate analyte species along the longitudinal axis of the first elongated separation channel;

a detector configured for detecting analyte species in said first separation channel, said detector being positioned intermediate the first and second ends of said first separation channel.

53. (currently amended) A system as in claim 52, further comprising:



a steering valve in fluid communication with the first separation channel, said steering valve comprising a connecting channel and configured to selectively divert fluid containing analyte species from said first separation channel at a location intermediate the first and second ends of the first separation channel into the connecting channel;

a second separation channel adapted for containing electrolyte fluid and analyte species, said second separation channel having a longitudinal axis and a first end and a second end, said second separation channel being in fluid communication with the connecting channel of said steering valve at a location intermediate said first and second ends, and, ~~said second separation channel further comprising a second~~

an electric field generator configured for moving analyte species along the second separation channel by at least one of electrophoretic migration and electroosmotic flow.

54. (original) A system as in claim 53, further comprising an analyte concentrator located in said second separation channel intermediate the first and second ends.

55. (original) A system as in claim 54, wherein said analyte concentrator comprises a line source of electric ~~electro~~ potential and an isolated ground, whereby an electric field generated by the second electric field generator can be locally altered so as to focus an analyte species at a location intermediate the first and second ends of the second separation channel.

56. (original) A system as in claim 55, further comprising a first electrode positioned at a first point along the longitudinal axis of the second separation channel, said first electrode being connected to said isolated ground, and a second electrode positioned at a second point along said

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longitudinal axis of the second separation channel, said second electrode being connected to a source of potential, said source of electro potential being also connected to the isolated ground.

57. (original) The system of claim 56, further comprising an analyte species detector positioned intermediate said first electrode and said second electrode.

58. (previously added by preliminary amendment) A liquid-phase electromobility focusing separation system configured to separate at least one discrete analyte species from an analyte sample, comprising:

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a first separation channel defined by a confinement enclosing an interior channel volume, said first separation channel having first and second ends and a longitudinal axis, and said first separation channel being configured to contain an electrolyte solution within the interior channel volume, said separation channel providing a common flowpath for both the analyte sample and the electrolyte solution;

a continuous electric field intensity gradient generator, further comprising a continuously variable resistor disposed adjacent said separation channel, said continuous electric field intensity gradient generator being configured to apply a electric field intensity gradient within the first separation channel along the longitudinal axis over at least a portion of the first separation channel intermediate the first and second ends, the intensity of electric field generated varying as a continuous function of location along the longitudinal axis, whereby electrophoretic migration of an analyte species within the first separation channel is actuated by a force that varies with position along the longitudinal axis as a continuous function of position along the longitudinal axis within said portion of the first separation

channel;

a fluid flow generator configured to generate a fluid flow along the longitudinal axis of the first separation channel, which flow is controllable and is configured to provide a force on the analyte species acting in opposition to the electric field intensity gradient, to enhance separation of said at least one analyte species by enabling separation control of an interaction of forces created by the continuous electric field intensity gradient generator and the fluid flow generator.

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59. (previously added by preliminary amendment) A system in accordance with claim 58, wherein the fluid flow generator further comprises a pump fluidly connected to the separation channel, said pump being configured to provide a pump-induced fluid flow through the separation channel to provide a counter-balancing hydro-dynamic force.

60. (previously added by preliminary amendment) An electromobility focusing separation system configured to separate analyte species in a fluid sample containing at least one analyte species, comprising:

a first separation channel defined by a containment forming a first elongated separation channel chamber having a longitudinal axis and first end and a second end, said containment configured to contain the fluid sample in the first elongated separation channel chamber,

an electrolyte solution contained within the first separation channel

an anode adjacent and in fluid communication with the first end of the first elongated separation channel chamber,

a cathode adjacent and in fluid communication with the second end of the first elongated separation channel chamber,

a first power supply in electric communication with the anode and the cathode and configured to provide an electrical potential there between, whereby electrophoretic migration of analyte species is enabled,

a sample injection port coupled to the separation channel, the sample injection port being in fluid communication with the electrolyte solution and enabling injection of a fluid sample containing one or more analyte species into the electrolyte solution,

a resistor disposed parallel and in fluid communication with the first elongated separation channel chamber along at least a portion of said first elongated separation channel chamber intermediate the first and second ends thereof, said resistor having a variable resistance varying as a function of position along the longitudinal axis of said first elongated separation channel chamber; and,

a fluid flow generator configured to provide a relative counter bulk flow of the electrolyte solution,

whereby electrophoretic migration of analyte species is effected by an electric field intensity which varies as a continuous function of position along the longitudinal axis of said first elongated separation channel chamber at locations adjacent the resistor, and electrophoretic migration of analyte species and bulk flow of the electrolyte solution can combine to separate analyte species along the longitudinal axis of the first elongated separation channel.

61. (previously added by preliminary amendment) A system in accordance with claim 60,